Breast Cancer Subtype Variation by Race and Ethnicity in a Diverse Population in British Columbia

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Abstract

The distribution of breast cancer subtypes varied significantly by race/ethnicity within our cross-sectional cohort from a multicultural population. Our data suggest that race/ethnicity plays a significant role in the biology of invasive breast cancer and that certain groups might experience different outcomes. These results have important implications for resource allocation and clinical care in multiethnic settings with universal healthcare.

Background: Breast cancer subtypes occur differentially across different racial and ethnic groups. However, their distribution within a multicultural population is unknown. **Materials and Methods:** Patients with invasive breast cancer newly diagnosed in 2006 and referred to the British Columbia Cancer Agency were identified from the Breast Cancer Outcomes Unit database. Race/ethnicity data were abstracted from a patient-completed health assessment questionnaire completed at the initial consultation, and grouped as white, East Asian, Aboriginal, South Asian, Southeast Asian, and other. Breast cancer subtypes were created using available data on estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) status. **Results:** A total of 1829 women had complete data. Of these women, 73% were white, 8% were East Asian, 4% Aboriginal, 3% South Asian, 3% Southeast Asian, and 3% other. The median age at diagnosis was 60 years; the youngest were Southeast Asian (51 years) and the oldest were white (60 years; $P < .001$). The overall ER positivity rate was 81%, highest in East Asian women (89%) and lowest in South Asian women (73%). The HER2 positivity rate was 16% for all patients and was highest in the South Asian (28%), Southeast Asian (28%), and Aboriginal (24%) women and lowest in the white women (14%; $P < .001$). Triple-negative (ER-, PR-, and HER2-negative) breast cancer was uncommon in East Asian women (5%) but more common in South Asian women (19%; $P < .001$). The 5-year breast cancer-specific survival was 90% (95% confidence interval, 89%-92%), with no significant difference among the racial/ethnic groups ($P = .136$). **Conclusion:** Breast cancer subtypes varied by race/ethnicity in our cross-sectional cohort of a multicultural population, suggesting that race/ethnicity plays a significant role in the biology of invasive breast cancer.

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Introduction

Since the initial description of breast cancer subtypes by Perou et al[1] in 2000, our concept of breast cancer has evolved to a better understanding of the unique biology, response, and prognosis of the specific cancer subtypes. Various reports have suggested that the distribution of breast cancer subtypes varies by race/ethnicity. For example, epidemiologic data have suggested an increased prevalence of human epidermal growth factor receptor 2 (HER2)-positive breast cancer in Asians living in the United States.[2,3] Specifically, HER2-positive breast cancer appears to be overrepresented in Chinese, Korean, Filipino, and Vietnamese women compared with non-Hispanic white women.[4] Population-based studies have also suggested a greater prevalence of basal-like cancer in African[5] and African-American women[6-8] and in a number of other countries, including Brazil.[9]

Simultaneously, race/ethnicity has been associated with different breast cancer outcomes in retrospective and prospective studies that have not evaluated breast cancer subtypes. Compared with white

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women, African-American women present with a more advanced stage at diagnosis,[10,11] higher grade tumors,[12] and worse survival after controlling for prognostic factors.[13,14] The age-adjusted breast-cancer specific mortality rate in the United States in 2010 for white women was 21.3 per 100,000 compared with 30.2 per 100,000 in black women.[15] However, the differences in the clinical outcomes among racial/ethnic groups are likely multifactorial, including socioeconomic factors, access to screening programs and treatment, inherent ethnic biology, and variable distributions of breast cancer subtypes.

British Columbia (BC) is a multiethnic province with a predominantly white population and a significant proportion of East Asian, Aboriginal, South Asian, and Southeast Asian individuals. Residents of BC have access to universal, publicly funded healthcare, including breast cancer screening, diagnosis, and treatment. The objective of the present study was to assess the distribution of breast cancer subtypes by race/ethnicity in our population and evaluate whether race/ethnicity is associated with different breast cancer outcomes.

Materials and Methods

Study Population

All patients diagnosed with invasive breast cancer from January 1, 2006 to December 31, 2006 were identified in the Breast Cancer Outcomes Unit (BCOU) database. The year 2006 was chosen for 3 reasons. First, 2006 was the first year when HER2 testing was consistently performed on all new breast cancer biopsy specimens at our institution. Second, that year allowed a sufficient follow-up length to examine the 5-year survival outcomes. Finally, the race/ethnicity data were extracted manually from the paper medical records, posing incremental logistical and resource challenges if additional years were included. The BCOU database is a population-based registry that contains prospectively collected demographic, pathologic, staging, and initial treatment data for patients referred to the BC Cancer Agency (BCCA) for breast cancer management. The outcomes for all patients were obtained by an active letter of follow-up to the general practitioners and through periodic direct linkage to the provincial vital statistics agency. The outcomes information collected included first local, regional, and distant relapse and, if applicable, the date and cause of death.

Baseline Characteristics and Breast Cancer Subtypes

Variables, including breast cancer subtype, patient age, tumor grade, and tumor stage, were obtained from the BCOU database. The patients' height and weight, measured at the initial consultation, were abstracted from the medical records to calculate the body mass index (BMI) for each patient.

The breast cancer subtype was assigned using standard immunohistochemistry (IHC) to determine the estrogen receptor (ER), progesterone receptor (PR), and HER2 status on core biopsy or excision specimens. HER2 was considered positive if the IHC score was 3+ or if the HER2-to-chromosome 17 centromere ratio was $\geq$ 2 using fluorescent in situ hybridization (FISH). FISH was only performed in cases with indeterminate or inconclusive HER2 expression by IHC. For the present study, the combinations of IHC markers and FISH data were used as surrogates for the following intrinsic breast cancer subtypes: luminal A or B (ER+ or PR+, HER2−), HER2 enriched (ER+ or ER− or PR+ or PR−, and HER2+), and basal-like (ER−, PR−, and HER2−). The distinction between luminal A and B subtypes was not made using the available IHC results.

Race and Ethnicity

At the initial consultation at a BCCA center, all patients completed the Health Assessment Form (HAF). The HAF explores patients' medical and sociodemographic background, including self-reported race/ethnicity through the question "To which ethnic or cultural group do you belong?" Each patient was asked to self-assign to 1 of the following major groups: Aboriginal (eg, North American First Nations, Inuit, Metis), black (eg, African, Haitian), white or European, Latin American, or Asian. The Asian group was further subdivided geographically into West Asian (Arab), East Asian (Chinese, Japanese, Korean), South Asian (East Indian, Pakistani), and Southeast Asian (Indonesian, Laotian, Filipino). Patients were assigned an "other" ethnicity if they listed $\geq$ 2 ethnicities (mixed heritage) or if they self-identified with a category not listed (eg, Pacific Islander). Patients with incomplete data were excluded. For the present analysis, patients were grouped into the following 6 categories: white, East Asian, Aboriginal, South Asian, Southeast Asian, and other.

Statistical Analysis

The main study endpoint was the distribution of breast cancer subtypes according to race/ethnicity, reported as frequencies. The proportion of ER+ and HER2+ cases according to breast cancer subtype was also calculated. Categorical variables were compared among the ethnic groups using the χ^2 test and continuous variables using the Kruskal-Wallis test. Because this was a retrospective, population-based study, no formal sample size calculations were performed.

As a secondary endpoint, breast cancer-specific survival (BCSS) was calculated as the time from the date of diagnosis to death from a primary or secondary cause related to breast cancer. Patients who were alive at the last follow-up visit or who had died of non−breast cancer causes were censored at the last follow-up visit. Overall survival (OS) was calculated from the date of the initial diagnosis to the date of the last follow-up visit or death from any cause. BCSS and OS were estimated using the Kaplan-Meier method and compared among groups using the log-rank test. The 5-year BCSS and OS rates are presented by ethnic group and breast cancer subtype with the 95% confidence intervals (CIs).

Cox proportional hazards regression models were used to examine the relationship between race/ethnicity and survival outcomes, adjusted for breast cancer subtype, stage, and grade and patient factors, including age, smoking history, and BMI. Treatment information was not included in the Cox regression model, because it was not available. The proportional hazards assumption was examined using Schoenfeld residual plots, and the sensitivity of the results to departures from this assumption was assessed using models stratified by any terms of concern.

All data analysis was performed using SAS, version 9.3, and the R statistical language, version 2.15. The University of BC/BCCA research ethics board approved the present study.